Summer 2020

The Importance of Understanding Pheochromocytomas

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Pheochromocytoma

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Pathophysiology of Pheochromocytomas

- Pheochromocytomas are neuroendocrine tumors that have their origins in the adrenal medulla chromaffin cells (Soltani et al., 2017).
- The chromaffin cells are part of the sympathetic nervous system and are responsible for secreting catecholamines into systemic circulation (Soltani et al., 2017).
- These catecholamines are epinephrine (80%) and norepinephrine (20%). In high concentrations, these hormones can cause unregulated hypertension (Soltani et al., 2017).
- Pheochromocytomas can be classified into 3 different categories based on what catecholamine they secrete.

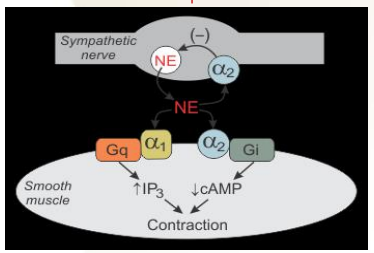
1. Epinephrine-secreting tumor
2. Norepinephrine-secreting tumor
3. Dopamine-secreting tumor

(Soltani et al., 2017)

- These catecholamines have varying effects on different receptors throughout the body. Primarily, the receptors that are clinically significant are the beta adrenergic receptors and alpha adrenergic receptors (Soltani et al., 2017).
- Stimulation of the beta adrenergic receptors by these catecholamines causes increased contractility and heart rate (Soltani et al., 2017).
- Stimulation of alpha adrenergic receptors induces vasoconstriction, resulting in hypertension (Soltani et al., 2017).
- The myocardium is sensitive to these catecholamines and chronic exposure can result in myocardial fibrosis (Soltani et al., 2017).
- Thus it is important to recognize these tumors early and intervene so that long-lasting effects are not permanent (Soltani et al., 2017).
- Epinephrine-secreting tumors can stimulate beta 2 adrenergic receptors which will cause vasodilatation instead of vasoconstriction. Vasodilatation can result in episodes of hypotension (Soltani et al., 2017).
- This is an important fact to remember because the majority of pheochromocytomas secrete norepinephrine, which primarily stimulates alpha adrenergic receptors, causing vasoconstriction and hypertension (Soltani et al., 2017).
- Immature tumors are sometimes missing dopamine β-hydroxylase, which is the converting enzyme of dopamine to norepinephrine (Soltani et al., 2017).
- Thus, dopamine-secreting pheochromocytomas may be found. These tumors indicate a higher likelihood of malignancy (Soltani et al., 2017).
- Pheochromocytomas can release norepinephrine, dopamine or epinephrine continuously or paroxysmally (Soltani et al., 2017).
- The sudden release of these catecholamines from pheochromocytomas typically cause hypertension, headache and diaphoresis (Soltani et al., 2017).
- This triad of symptoms is known as "an attack" (Soltani et al., 2017).

Clinical Presentation

- Roughly 10-40% of pheochromocytomas are not found due to symptomatology. In these cases, the tumors are found during unrelated imaging (Ramachandran & Rewari, 2017).
- The classic triad of symptoms are headache, heart palpitations and diaphoresis (Ramachandran & Rewari, 2017). These symptoms are found in roughly 40% of patients.
- Pheochromocytomas have been referred to as "the Great Mimic" due to their similarities to many other illnesses (Soltani et al., 2017).
- Patients present to their primary care physicians with complaints of weakness, panic attacks, nausea and vomiting, and the classic triad (Paknikar, 2015).
- One of the main factors that clinicians consider is the episodic nature of pheochromocytomas. Most pheochromocytomas that cause symptoms will do so in paroxysmal fashion (Lenders & Eisenhofer, 2017).



(Klabunde, 2013)

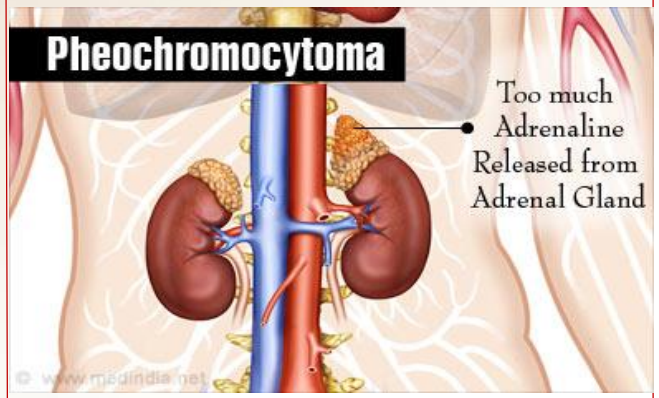
Figure 2 illustrates the physiological action that norepinephrine exerts on alpha adrenergic receptors located in smooth muscle. Stimulation of the alpha 1 adrenergic receptor by norepinephrine results in contraction of smooth muscle lining the walls of blood vessels, leading to an increase in blood pressure (Klabunde, 2013).

The Importance of Understanding Pheochromocytomas

Introduction

- Pheochromocytomas are rare neuroendocrine tumors that originate from chromaffin cells in the adrenal medulla (Tian et al., 2019).
- These tumors can have vast and devastating effects on a patient's cardiovascular system, potentially leading to hemodynamic instability (Tian et al., 2019).
- They exert their effects by releasing catecholamines, such as norepinephrine, into the bloodstream, which leads to labile fluctuations in a patient's blood pressure (Tian et al., 2019).
- In 1937, Dr. Charles Mayo was the first to clinically diagnose and surgically remove a pheochromocytoma tumor (Mubarik & Aeddula, 2020).
- Although pheochromocytoma tumors are rare, they pose an incredible risk to a patient's outcome if not treated properly (Fermandois et al., 2020).
- Nurse anesthetists need to understand the pathophysiology of these tumors so that they can adequately and safely manage the hemodynamic fluctuations that can be seen.

Illustration depicting a Pheochromocytoma



(Paknikar, 2015)

Figure 1 depicts the origin of pheochromocytomas. These tumors arise from the adrenal glands that sit on top of the kidneys (Soltani et al., 2017). Because these tumors stem from chromaffin cells within the adrenal medulla, they can oversecrete endogenous catecholamines into the systemic circulation (Soltani et al, 2017). Overproduction of catecholamines can lead to significant episodes of hypertension, tachycardia, and diaphoresis (Mubarik & Aeddula, 2020).

The main treatment for pheochromocytomas is surgical removal (Lenders & Eisenhofer, 2017). Thus, it is of utmost importance that the anesthesia provider understands the pathological process of these tumors. Without proper knowledge and treatment plan, pheochromocytomas can cause catastrophic hemodynamic instability in the anesthetized patient (Lenders & Eisenhofer, 2017).

Diagnosis

- Pheochromocytomas are diagnosed based on blood and urine tests (Paknikar, 2015).
- Catecholamines in the body are broken down into inactive metabolites by enzymes (Paknikar, 2015).
- These metabolites, metanephrine and normetanephrine, can be detected at elevated levels in the blood and urine (Paknikar, 2015).
- Before the tests are performed, patients are advised to avoid certain drugs such as tricyclic antidepressants and acetaminophen due to their ability to skew results (Paknikar, 2015).
- Additionally, imaging such as CT scans and MRI can be used to detect the tumor and assess whether it has spread (Paknikar, 2015).

Treatment

- Pheochromocytomas can be surgically removed to prevent the release of catecholamines and reduce the risk of malignancy and metastatsis (Tauzin-Fin et al., 2019).
- Patients with symptomatic and unpredictable pheochromocytomas must receive medical management between 10-14 days before surgery (Garica et al., 2019).
- Medical management involves the administration of phenoxybenzamine, a noncompetitive and nonselective alpha-blocking agent (Garcia et al., 2019).
- Phenoxybenzamine will prevent the tumor's secretion of excess catecholamines from causing extensive vasoconstriction, resulting in hypertension (Tauzin-Fin et al., 2019).
- Beta adrenergic receptor blockade is also established to prevent tachyarrythmias from occurring during surgery (Garcia et al., 2019).
- During medical management it is of utmost importance to block the alpha-adrenergic effects of the catecholamines before administering a beta adrenergic receptor blocker due to the risk of acute cardiac failure as a s result of unopposed vasoconstriction (Garcia et al., 2019).

Risk Factors

- Current literature states that the exact cause of pheochromocytomas is unknown but several genes have been associated with its occurrence (Paknikar, 2015).
- Mubarik and Aeddula et al. (2020) suggests that roughly 90% of cases are random with no definitive link.
- Additionally, 10% can be linked to familial inheritance or the presence of syndromes like Von Hippel–Lindau syndrome, type 1 neurofibromatosis, and multiple endocrine neoplasia syndromes type IIA and type IIB with an autosomal dominant mode of transmission (Mubarik & Aeddula, 2020).

Anesthesia Considerations

- Surgery to remove a pheochromocytoma is considered a high-risk surgery due to the possibility of hemodynamic instability (Garcia et al., 2019).
- Constant communication between the surgical and anesthesia team is important to relay information such as initial incision, division of blood supply from tumor and any manipulation of the tumor (Garcia et al., 2019).
- Blood pressure fluctuations is one of the most important vital signs to monitor, thus invasive monitoring with an arterial line is needed (Garcia et al., 2019).
- Central venous access may be warranted due to the many types of medications, fluids and monitoring that is required (Garcia et al., 2019).
- The fluid volume status of the patient should be monitored carefully. Underhydration could result in significant hypotension, while overhydration could result in cardiac failure and pulmonary edema (Garcia et al., 2019).
- Important medications to have ready are vasodilators, vasoconstrictors, anti-arrythmias such as lidocaine, and fluids (Garcia et al., 2019).

References

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